Friday
May 20, 1988

Part II

Environmental Protection Agency

Twenty-second Report of the Interagency Testing Committee to the Administrator; Receipt of Report and Request for Comments Regarding Priority List of Chemicals; Notice

40 CFR Parts 712 and 716

Preliminary Assessment Information and Health and Safety Data Reporting; Addition of Chemicals; Final Rule

ENVIRONMENTAL PROTECTION AGENCY

[OPTS-41029; FRL-3381-7]

Twenty-second Report of the Interagency Testing Committee to the Administrator; Receipt of Report and Request for Comments Regarding Priority List of Chemicals

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: The Interagency Testing Committee (ITC), established under section 4(e) of the Toxic Substances Control Act (TSCA), transmitted its Twenty-Second Report to the Administrator of EPA on May 2, 1988. This report, which revises and updates the Committee's priority list of chemicals, adds 10 chemicals to the list for priority consideration by EPA in promulgation of test rules under section 4(a) of the Act. The Twenty-Second Report is included with this notice. One chemical, 1,6-hexamethylene diisocyanate (CAS No. 822-06-0) is designated for response within 12 months. In response to ITC's designation, EPA will either initiate rulemaking under section 4(a) of TSCA, or publish a **Federal Register** notice explaining the reasons for not initiating such rulemaking within 12 months. Crotonaldehyde (CAS No. 4170-30-3); imidazolium quaternary ammonium compounds (CAS No. 68122-86-1); and seven ethoxylated quaternary ammonium compounds (CAS Nos. 68153-35-5, 68389-88-8, 68389-89-9, 68410-69-5, 68413-04-7, 68554-06-3, and 70914-090-9) are not designated for response within 12 months. EPA invites interested persons to submit written comments on the report, and to attend Focus Meetings to help narrow and focus the issues raised by the ITC's recommendations.

Additionally, EPA is soliciting interest in public participation in the consent agreement process for crotonaldehyde, imidazolium quarternary ammonium compounds, and seven ethoxylated quaternary ammonium compounds.

The ITC also has removed 9 chemicals from the priority list. Six aminoanthraquinone dyes (CAS Nos. 128-86-9, 2861-02-1, 6247-34-3, 6424-85-7, 12217-79-7 and 17418-58-5) have been removed from the list on the basis of relatively low aggregate production and sufficient genotoxicity testing to reduce concerns about these chemicals. Tributyl phosphate (CAS No. 126-73-8), isopropanol (CAS No. 67-63-0), and methyl *tert* butyl ether (CAS No. 1634-04-4) have been removed because EPA has responded to the ITC's previous recommendations for testing of the chemicals.

DATES: Written comments should be submitted by June 20, 1988. Submit written notice of interest in being designated an "interested party" to development of consent agreements for crotonaldehyde, imidazolium quaternary ammonium compounds and seven ethoxylated quaternary ammonium compounds by June 20, 1988. Focus Meetings will be held on June 14 and June 17, 1988.

ADDRESS: Send written submissions to: TSCA Public Docket Office (TS-793), Office of Toxic Substances, Environmental Protection Agency, Rm. NE G-004, 401 M Street SW., Washington, DC 20460.

Submissions should bear the document control number (OPTS-41029).

The public record supporting this action, including comments, is available for public inspection in Rm. NE G-004 at the address noted above from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays. The Focus Meetings will be held at EPA Headquarters, Rm. 103 NE Mall, 401 M Street SW., Washington, DC. Persons planning to attend the Focus Meetings, and/or seeking to be informed of subsequent public meetings on these chemicals, should notify the TSCA Assistance Office at the address listed below. To ensure seating accommodations at the Focus Meetings, persons interested in attending are asked to notify EPA at least one week ahead of the scheduled date.

FOR FURTHER INFORMATION CONTACT: Michael M. Stahl, Acting Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Environmental Protection Agency, 401 M Street SW., Washington, DC 20460, (202) 554-1404.

SUPPLEMENTARY INFORMATION: EPA has received the Report of the TSCA Interagency Testing Committee to the Administrator.

I. Background

TSCA (Pub. L. 94-469, 90 Stat. 2003 *et seq*; 15 U.S.C. 2601 *et seq.*) authorizes the Administrator of EPA to promulgate regulations under section 4(a) requiring testing of chemical substances and mixtures in order to develop data relevant to determining the risks that such chemical substances and mixtures may present to health and the environment. Section 4(e) of TSCA established an Interagency Testing Committee to make recommendations to the Administrator of EPA on chemical substances and mixtures to be given priority consideration in proposing test rules under section 4(a). Section 4(e) directs the ITC to revise its list of recommendations at least every 6 months as necessary. The ITC may "designate" up to 50 substances and mixtures at any one time for priority consideration by the Agency. The chemical 1,6-hexamethylene diisocyanate is a designated chemical. For such designations, the Agency must within 12 months either initiate rulemaking or issue in the **Federal Register** its reasons for not doing so. The ITC's Twenty-Second Report was received by the Administrator on May 2 and follows this Notice. The Report adds 10 substances to the TSCA section 4(e) priority list.

II. Written and Oral Comments and Public Meetings

EPA invites interested persons to submit detailed comments on the ITC's new recommendations. The Agency is interested in receiving information concerning additional or ongoing health and safety studies on the subject chemicals as well as information relating to the human and environmental exposure to these chemicals.

A notice is published elsewhere in today's **Federal Register** adding 8 of the 10 substances recommended in the ITC's Twenty-Second Report to the TSCA section 8(d) Health and Safety Data Reporting Rule (40 CFR Part 716). Two of the 10 substances, 1,6-hexamethylene diisocyanate (52 FR 16022, May 1, 1987) and crotonaldehyde (51 FR 2890, January 22, 1986), already are subject to this rule, which requires the reporting of unpublished health and safety studies on the listed chemicals. All 10 chemicals will be added to the TSCA section 8(a) Preliminary Assessment Information Rule (40 CFR Part 712) published elsewhere in this issue. The section 8(a) rule requires the reporting of production volume, use, exposure, and release information on the listed chemicals.

Focus Meetings will be held to discuss relevant issues pertaining to these chemicals and to narrow the range of issues/effects which will be the focus of the Agency's subsequent activities in responding to the ITC recommendations. The Focus Meetings will be held as follows:

June 14, 1988

9:30 a.m.—Imidazolium quaternary ammonium compounds
1:00 p.m.—Ethoxylated quaternary ammonium compounds

June 17, 1988

9:30 a.m.—Crotonaldehyde
1:00 p.m.—1,6-Hexamethylene diisocyanate

They will be held at EPA Headquarters, Rm. 103 NE Mall, 401 M Street SW., Washington, DC. These meetings are intended to supplement and expand upon written comments submitted in response to this notice.

Persons wishing to attend these meetings, or subsequent meetings on these chemicals, should call the TSCA Assistance Office at the telephone number listed above at least one week in advance.

This notice also serves to invite persons interested in participating in or monitoring negotiations for consent agreements for crotonaldehyde, imidazolium quaternary ammonium compounds, and ethoxylated quaternary ammonium compounds to notify EPA no later than June 20, 1988. The procedures for negotiations are described in 40 CFR 790.22. All written submissions should bear the identifying docket number (OPTS–41029).

III. Status of List

In addition to adding the 10 recommendations to the priority list, the ITC's Twenty-Second Report notes the removal of 9 chemicals from the list since the last ITC report. Six aminoanthraquinone dyes have been removed from the list by the ITC on the basis of relatively low aggregate production and sufficient genotoxicity testing to reduce concerns. Subsequent to ITC's preparation of its Twenty-First Report, EPA responded to the ITC's recommendations for three additional chemicals. The three chemicals removed and the dates of publication in the **Federal Register** of EPA's responses to the ITC for these chemicals are: tributyl phosphate (52 FR 43346, November 12, 1987); isopropanol, (53 FR 8638, March 16, 1988); and methyl *tert* butyl ether (53 FR 10391, March 31, 1988).

The current list contains 1 designated substance, 2 chemicals recommended with intent-to-designate, and 14 recommended substances.

Authority: 15 U.S.C. 2603.

Dated: May 11, 1988.

J. Merenda,

Director, Existing Chemical Assessment Division.

Twenty-Second Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency

Summary

Section 4 of the Toxic Substances Control Act of 1976 (TSCA, Pub. L. 94–469) provides for the testing of chemicals in commerce that may present an unreasonable risk of injury to health or the environment. It also provides for the establishment of a Committee (ITC), composed of representatives from eight designated Federal agencies, to recommend chemical substances and mixtures (chemicals) to which the Administrator of the U.S. Environmental Protection Agency (EPA) should give priority consideration for the promulgation of testing rules.

Section 4(e)(1)(A) of TSCA directs the Committee to recommend to the EPA Administrator chemicals to which the Administrator should give priority consideration for the promulgation of testing rules pursuant to section 4(a). The Committee is required to designate those chemicals, from among its recommendations, to which the Administrator should respond within 12 months by either initiating a rulemaking proceeding under section 4(a) or publishing the Administrator's reason for not initiating such a proceeding. At least every 6 months, the Committee makes those revisions in the TSCA section 4(e) Priority List that it determines to be necessary and transmits them to the EPA Administrator.

As a result of its deliberations, the Committee is revising the TSCA section 4(e) Priority List by the addition of 10 chemicals.

The Priority List is divided into three parts: Part A contains those recommended chemicals and groups designated for priority consideration and response by the EPA Administrator within 12 months. Part B contains chemicals and groups of chemicals recommended with intent-to-designate. This category was established by the Committee in its seventeenth report (50 FR 47603; November 19, 1985) to take advantage of rules promulgating automatic reporting requirements for non-designated ITC recommendations under the section 8(a) Preliminary Assessment rule and the TSCA section 8(d) Health and Safety Data Reporting rule. Information received following recommendation with intent-to-designate may influence the Committee to either designate or not designate the chemicals or groups of chemicals in a subsequent report to the Administrator. Part C contains chemicals and groups of chemicals that have been recommended for priority consideration by EPA without being designated for response within 12 months. The changes to the Priority List are presented, together with the types of testing recommended, in the following Table 1:

TABLE 1—ADDITIONS TO THE SECTION 4(e) PRIORITY LIST, MAY 1988

Chemical/Group	Recommended studies
A. *Designated for response within 12 months:*	
1,6-Hexamethylene diisocyanate [1] CAS No. 822-06-0.	Health Effects: Chronic toxicity, including oncogenicity; reproductive and developmental effects.
	Chemical Fate: None
	Ecological Effects: None
B. *Recommended with Intent-to-Designate:*	
Crotonaldehyde [2] CAS No. 4170-30-3.	Health Effects: None
	Chemical Fate: Volatilization rate from water; aerobic aquatic biodegradation rate.
	Ecological Effects: Acute toxicity to algae, fish and aquatic invertebrates.
C. *Recommended Without Being Designated for Response Within 12 Months:*	
Imidazolium Quaternary Ammonium Compounds [3] (CAS No. 68122-86-1).	Health Effects: Chronic toxicity studies to evaluate potential effects through long-term dermal exposures.
	Chemical Fate: Aerobic and anaerobic biodegradation of the chemical sorbed to freshwater and estuarine sediments.
	Ecological Effects: Acute and chronic effects on representative freshwater and estuarine benthic organisms.
Ethoxylated Quaternary Ammonium Compounds [4] (CAS Nos. 68153-35-5, 68389-88-8, 68389-89-9, 68410-69-5, 68413-04-7, 68554-06-3, and 70914-09-9).	Health Effects: Chronic toxicity studies to evaluate potential effects through long-term dermal exposures.
	Chemical Fate: Aerobic and anaerobic biodegradation of the chemicals sorbed to freshwater and estuarine sediments.
	Ecological Effects: Acute and chronic effects on representative freshwater and benthic organisms.

CA Index Names (9 CI)

[1] Hexane, 1,6-diisocyanato-.

[2] 2-Butenal.

[3] Imidazolium compounds, 4,5-dihydro-1-methyl-2-hortallow alkyl-1-(2-tallow amidoethyl), Me sulfates.

[4] Ethanaminium, 2-amino-N-(2-aminoethyl)-N-(2-hydroxyethyl)-N-methyl-, N,N'-ditallow acyl derivs., Me sulfates (salts); CAS No. 68153-35-5, Poly(oxy-1,2-ethanediyl), α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-dicoco acyl derivs., Me sulfates (salts); CAS No. 68389-88-8, Poly(oxy-1,2-ethanediyl), α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-

bis(hydrogenated tallow acyl) derivs., Me sulfates (salts); CAS No. 68389-89-9,

Poly(oxy-1,2-ethanediyl), α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-ditallow acyl derivs., Me sulfates (salts); CAS No. 68410-69-5,

Poly[oxy(methyl-1,2-ethanediyl)], α-[2-[bis(2-aminoethyl)-methylammonio]-methylethyl]-ω-hydroxy-, N,N'-, ditallow acyl derivs., Me sulfates (salts); CAS No. 68413-04-7,

Poly(oxy-1,2-ethanediyl), α-[3-[bis(2-aminoethyl)-methylammonio]-2-hydroxypropyl]-ω-hydroxy-, N-coco acyl derivs., Me sulfates (salts); CAS No. 68554-06-3, and

Poly(oxy-1,2-ethanediyl), α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-di-C_{14-18} acyl derivs., Me sulfates (salts); CAS No. 70914-09-9

TSCA Interagency Testing Committee

Statutory Member Agencies and Their Representatives

Council on Environmental Quality
Joseph Jehl, Member [1]
Department of Commerce
Partick D. Cosslett, Member
Raimundo Prat, Alternate
Environmental Protection Agency
John D. Walker, Member
Laurence S. Rosenstein, Alternate
National Cancer Institute
Richard Adamson, Member
Elizabeth K. Weisburger, Alternate
National Institute of Environmental Health Sciences
James K. Selkirk, Member and Chairperson
National Institute for Occupational Safety and Health
Bryan D. Hardin, Member and Vice Chairperson
Rodger L. Tatken, Alternate
National Science Foundation
Rodger W. Baier, Member
Jarvis L. Moyers, Alternate
Occupational Safety and Health Administration
Robert Turnage, Member [2]
Stephen Mallinger, Alternate

Liaison Agencies and Their Representatives

Consumer Product Safety Commission
Lakshmi C. Mishra
Department of Agriculture
Richard M. Parry, Jr.
Elise A. B. Brown
Department of Defense
Vacant
Department of the Interior
Sarah Gerould
Food and Drug Administration
Arnold Borsetti
National Library of Medicine
Vera Hudson
National Toxicology Program
Dorothy Canter

Committee Staff

Robert H. Brink, Executive Secretary
Norma Williams, ITC Program Specialist

Support Staff

Alan Carpien—Office of the General Counsel, EPA

The Committee acknowledges and is grateful for the assistance and support given the ITC by the staff of Dynamac Corporation (technical support contractor) and personnel of the EPA Office of Toxic Substances.

[1] Appointed on October 30, 1987.
[2] Appointed on October 26, 1987.

Chapter 1—Introduction

1.1 *Background.* The TSCA Interagency Testing Committee (Committee) was established under section 4(e) of the Toxic Substances Control Act of 1986 (TSCA, Pub. L. 94-469). The specific mandate of the Committee is to recommend to the Administrator of the U.S. Environmental Protection Agency (EPA) chemical substances and mixtures in commerce that should be given priority consideration for the promulgation of testing rules to determine their potential hazard to human health and/or the environment. TSCA specifies that the Committee's recommendations shall be in the form of a Priority List, which is to be published in the **Federal Register**. The Committee is directed by section 4(e)(1)(A) of TSCA to designate those chemicals on the Priority List to which the EPA Administrator should respond within 12 months by either initiating a rulemaking proceeding under section 4(a) or publishing the Administrator's reason for not initiating such a proceeding. There is no statutory time limit for EPA response regarding chemicals that ITC has recommended but not designated for response within 12 months.

At least every 6 months, the Committee makes those revisions in the section 4(e) Priority List that it determines to be necessary and transmits them to the EPA Administrator.

The Committee is composed of representatives from eight statutory member agencies and seven liaison agencies. The specific representatives and their affiliations are named in the front of this report. The Committee's chemical review procedures and priority recommendations are described in previous reports (Refs. 1 through 6).

1.2 *Committee's previous reports.* Twenty-one previous reports to the EPA Administrator have been issued by the Committee and published in the **Federal Register** (Refs. 1 through 6). Ninety-six entries (chemicals and groups of chemicals) were recommended for priority consideration by the EPA Administrator and designated for response within 12 months. In addition, fourteen chemicals and one group of chemicals were recommended without being so designated.

1.3 *Committee's activities during this reporting period.* Between October 16, 1987 and April 21, 1988, the Committee continued to review chemicals from its fifth and sixth scoring exercises, and from nominations by Member Agencies, Liaison Agencies and State Agencies.

The Committee contacted chemical manufacturers and trade associations to request information that would be of value in its deliberations. Most of those contacted provided unpublished information on current production, exposure, uses, and effects of chemicals under study by the Committee.

During this reporting period, the Committee reviewed available information on eighty-four chemicals. Ten were selected for addition to the section 4(e) Priority List, and twenty-four were deferred indefinitely. The remaining chemicals are still under study.

In its twentieth report to the EPA Administrator (Ref. 5, ITC, 1987), the Committee placed ethylbenzene (CAS No. 100-41-4) on the Priority List on the "Recommended with Intent-to-Designate" category. The Committee recommended that ethylbenzene be tested for acute toxicity to freshwater algae and invertebrates and to saltwater algae, invertebrates and fish. Subsequently, the Committee learned that acute toxicity testing of ethylbenzene with freshwater invertebrates had recently been completed at the University of Wisconsin. As noted in the twenty-first report, the Committee also was informed that a consortium of ethylbenzene producers, the Styrene and Ethylbenzene Association, voluntarily sponsored studies on the other acute toxicity tests recommended by the Committee. The Committee deferred a decision on whether or not to designate ethylbenzene pending a review of the data developed during the above studies. The Committee has reviewed the data developed in those studies and has concluded that all of the data gaps identified in the twentieth report have been satisfactorily resolved with the exception of saltwater invertebrate testing. Industry has volunteered to sponsor additional studies with saltwater invertebrates. The Committee has decided to continue to defer a decision on whether or not to designate ethylbenzene pending a review of data from the additional invertebrate tests.

In its twenty-first report to the EPA Administrator, the Committee

recommended genotoxicity testing on six aminoanthraquinone dyes (CAS Nos 128–86–9, 2861–02–1, 6247–34–3, 6424–85–7, 12217–79–7 and 17418–58–5). Subsequent to the recommendation the Committee had an opportunity to examine the TSCA section 8(a) Preliminary Assessment rule and TSCA section 8(d) Health and Safety Data Reporting rule information submitted to the EPA. That information included current production and use information on those dyes and additional data on genotoxicity tests. As a result of its review of that information, the Committee has concluded that the six aminoanthraquinone dyes with the above CAS numbers should be removed from the Priority List on the basis of relatively low aggregate production and sufficient genotoxicity testing to reduce concerns.

1.4 *The TSCA section 4(e) Priority List.* Section 4(e)(1)(B) of TSCA direct the Committee to: "* * * make such revisions in the [priority] list as it determines to be necessary and * * * transmit them to the Administrator together with the Committee's reasons for the revisions." Under this authority, the Committee is revising the Priority List by adding ten chemicals: 1,6-hexamethylene diisocyanate (CAS No. 822–06–0), crotonaldehyde (CAS No. 4170–30–3), imidazolium quaternary ammonium compounds (CAS No. 68122–86–1) and ethoxylated quaternary ammonium compounds (CAS Nos. 68153–35–5, 68389–88–8, 68389–89–9, 68410–69–5, 68413–04–7, 68554–06–3 and 70914–09–9). Nine chemicals are being removed from the Priority List at this time. Tributyl phosphate (CAS No. 126–73–8) was the subject of a Notice of Proposed Rulemaking (52 FR 43346; November 12, 1987). Isopropanol (CAS No. 67–63–0) also was the subject of a Notice of Proposed Rulemaking (53 FR 8638; March 16, 1988) and methyl *tert* butyl ether (CAS No. 1634–04–4) was the subject of a Testing Consent Order (53 FR 10391; March 31, 1988). In addition, six aminoanthraquinone dyes (CAS Nos. 128–86–9, 2861–02–1, 6247–34–3, 6424–85–7, 12217–79–7 and 17418–58–5) are being removed for the reasons given in section 1.3.

With the ten new recommendations and nine removals noted in this report, seventeen entries now appear on the section 4(e) Priority List. The Priority List is divided in the following Table 2 into three parts; namely, A. Chemicals and Groups of Chemicals Designated for Response Within 12 Months, B. Chemicals and Groups of Chemicals Recommended with Intent-to-Designate, and C. Chemicals and Groups of Chemicals Recommended Without Being Designated for Response Within 12 Months. Table 2 follows:

TABLE 2—THE TSCA SECTION 4(e) PRIORITY LIST, MAY 1988

Entry	Date of designation
A. Chemicals and Groups of Chemicals Recommended and Designated for Response Within 12 Months:	
1. 1,6-Hexamethylene diisocyanate.	May 1988
B. Chemicals and Groups of Chemicals Recommended with Intent-to-Designate:	
1. Ethylbenzene	May 1987
2. Crotonaldehyde	May 1988
C. Chemicals and Groups of Chemicals Recommended Without Bein Designated for Response Withi 12 Months:	
1. Diisodecyl phenyl phosphite	Nov. 1985
2. C.I. Disperse Blue 79	Nov. 1986
3. Methyl ethyl ketoxime	Nov. 1986
4. *N*-[5-[bis[2-(acetyloxy)ethyl]amino]-2-[(2-bromo-4,6-dinitrophenyl)azo]-4-methoxy phenyl]-acetamide.	May 1987
5. *N*-[5-[bis[2-(acetyloxy)ethyl]amino]-2-[2-chloro-4,6-dinitrophenyl)azo]-4-methoxy phenyl]-acetamide.	May 1987
6. *N*-[5-[bis[2-(acetyloxy)ethyl]amino]-2-[(2-chloro-4,6-dinitrophenyl)azo]-4-ethoxy phenyl]-acetamide.	May 1987
7. Imidazolium compounds, 4,5 dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl), Me sulfates.	May 1988
8. Ethanaminium,2-amino-N-(2-aminoethyl)-N-(2-hydroxyethyl)-N-methyl-, N,N'-ditallow acyl derivs., Me sulfates (salts).	May 1988
9. Poly(oxy-1,2-ethanediyl),α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-dicoco acyl derivs., Me sulfates (salts).	May 1988
10. Poly(oxy-1,2-ethanediyl),α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-bis(hydrogenatec tallow acyl) derivs., Me sulfates (salts).	May 1988
11. Poly(oxy-1,2-ethanediyl),α-[2-[bis(2-aminoethyl)-methylammonio-ethyl]-ω-hydroxy-, N,N'-ditallow acyl derivs., Me sulfates (salts).	May 1988
12. Poly[oxy(methyl-1,2-ethanediyl)],α-[2-[bis(2-aminoethyl)-methylammonio]-methylethyl]-ω-hydroxy-, N,N'-, ditallow acyl derivs., Me sulfates (salts).	May 1988
13. Poly(oxy-1,2-ethanediyl),α-[3-[bis(2-aminoethyl)-methylammonio]-2-hydroxypropyl]-ω-hydroxy-, N-coco acyl derivs., Me sulfates (salts).	May 1988
14. Poly(oxy-1,2-ethanediyl),α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-di-C_{14-18} acyl derivs., Me sulfates (salts).	May 1988

References

(1) Sixteenth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, May 21, 1985, 50 FR 20930–20939. Includes references to Reports 1 through 15 and an annotated list of removals.

(2) Seventeenth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, November 19, 1985, 50 FR 47603–47612.

(3) Eighteenth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, May 19, 1986, 51 FR 18368–18375.

(4) Nineteenth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, November 14, 1986, 51 FR 41417–41432.

(5) Twentieth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, May 20, 1987, 52 FR 19020–19026.

(6) Twenty-first Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, November 20, 1987, 52 FR 44830–44837.

Chapter 2—Recommendations of the Committee

2.1 *Chemicals recommended for priority consideration by the EPA Administrator.* As provided by section 4(e)(1)(B) of TSCA, the Committee is adding the following chemical substances to the section 4(e) Priority List: 1,6-hexamethylene diisocyanate CAS No. 822–06–0), crotonaldehyde CAS No. 4170–30–3), imidazolium quaternary ammonium compounds (CAS No. 68122–86–1) and ethoxylated quaternary ammonium compounds (CAS Nos. 68153–35–5, 68389–88–8, 68389–89–9, 68410–69–5, 68413–04–7, 68554–06–3 and 70914–09–9). The recommendation of these chemicals is made after considering the factors identified in section 4(e)(1)(A) and other relevant information, as well as the professional judgment of Committee members.

2.2 *Chemicals designated for response within 12 months—*2.2.a *1,6-Hexamethylene diisocyanate—Summary of recommended studies.* It is recommended that 1,6-hexamethylene diisocyanate be tested for the following:

1. *Chemical fate:* None.

2. *Health effects:* Chronic toxicity including oncogenicity) and reproductive and developmental effects studies.

3. *Ecological effects:* None.

Physical and Chemical Information

CAS Number: 822-06-0
Synonyms: Hexane, 1,6-diisocyanato-; Hexamethylene diisocyanate; 1,6-Diisocyanatohexane
Acronym: HDI
Trade Names: Desmodur H; Mondur HX
Structural Formula: $OCNCH_2CH_2CH_2CH_2CH_2CH_2NCO$

$OCNCH_2CH_2CH_2CH_2CH_2CH_2NCO$

Empirical Formula: $C_8H_{12}N_2O_2$
Molecular Weight: 168.0
Appearance: Liquid
Boiling Point: 212.8 °C at 760 mmHg (Ref. 22, NIOSH, 1978)
Vapor Pressure: 0.05 mmHg at 24 °C (Ref. 22, NIOSH, 1978)
Specific Gravity: 1.04 (Ref. 22, NIOSH, 1978)
Flashpoint: 140 °C (Ref. 22, NIOSH, 1978)
Solubility: Poorly soluble in water; readily soluble in organic solvents (Ref. 22, NIOSH, 1978)
Log Octanol/Water Partition Coefficient (log P): −1.9 (Est'd., Ref. 14, Leo et al., 1971).

Rationale for Recommendations

I. Exposure Information

A. Production/Use/Disposal/Environmental Release

Hexamethylene diisocyanate (HDI) is produced in commercial quantities at Baytown, TX; current annual production is about 11 million pounds (Ref. 19, Mobay, 1988b). Laboratory quantities of HDI are also produced by Morton Thiokol, Inc. at its Danvers, MA plant (Ref. 10, ICF, 1986). The public portion of the TSCA Inventory lists U.S. production at 1 to 10 million pounds in 1977 (Ref. 27, USEPA, 1988). No import data are reported for HDI. In 1981, approximately 2 to 3 million pounds were exported (Ref. 16, Mobay, 1982).

The manufacturing process for HDI, similar to that of other diisocyanates, employs phosgenation of hexamethylene diamine. In response to a request for information, Mobay estimated that the quantity of HDI that enters the environment during production and use does not exceed 20,000 pounds per year (Ref. 16, Mobay, 1982).

HDI is used in the manufacture of higher molecular weight biuret polyisocyanate products. These are commercially used as curing agents in the formulation of polyurethane paint systems for automobile refinishing, industrial maintenance, marine coatings, and other higher performance coating systems (Ref. 16, Mobay, 1982).

B. Evidence for Human and Environmental Exposure

There is no OSHA permissible exposure level (PEL) for HDI. In 1978, NIOSH recommended that OSHA adopt the same standard also recommended for toluene diisocyanate (TDI) and methylene diphenyldiisocyanate (MDI), i.e., an 8-hour time-weighted average of 5 ppb (35 ug/m³) (Ref. 22, NIOSH, 1978). The recommended 10-minute short-term exposure limit is 0.02 ppm (140 ug/m³) (Ref. 22, NIOSH, 1978). ACGIH earlier recommended the same levels (Ref. 1, ACGIH, 1976). The level immediately dangerous to life and health (IDLH), beyond which irreversible health effects are known to occur, is 10 ppm (Ref. 28, Woolrich, 1982).

The National Occupational Hazard Survey (NOHS), conducted by the National Institute for Occupational Safety and Health (NIOSH) from 1972 to 1974, estimated that about 4,490 workers in 238 plants were exposed to HDI through manufacture, processing, or use in 1970. Of these, about 4,000 were involved with coating applications (Ref. 21, NIOSH, 1976). NIOSH also conducted a second workplace survey, the National Occupational Exposure Survey (NOES) from 1980 to 1983 (Ref. 23, NIOSH, 1984). Preliminary data from the NOES indicated that 39 workers, including 11 women, were potentially exposed in 1980.

The number of workers exposed to HDI is probably underestimated since it is impossible to estimate the workers in trade professions or other operations using products containing HDI. However, data indicate that coatings applications provide the greatest source of occupational exposure to HDI. Information obtained from the United Auto Workers suggests that 1,000 to 10,000 workers are potentially exposed to HDI-containing coatings and adhesives in new car manufacture (Ref. 26, UAW, 1988). The Automotive Services Association estimated that there are 60,000 to 100,000 private autobody and repaint shops that usually employ 1.5 to 12 persons each, potentially exposing between 90,000 and 1.2 million persons (Ref. 4, ASA, 1988). In a 1982 submission to the TSCA Interagency Testing Committee, Mobay estimated that 153,000 autobody repair workers were potentially exposed to HDI (Ref. 16, Mobay, 1982).

Information received from the International Brotherhood of Painters and Allied Trades (IBPAT) indicated that about 60,000 union members use an HDI-containing coating at least once a year. HDI-containing coatings are used several times a year by about 30,000 workers; 3,000 use HDI-containing paint exclusively (Ref. 9, IBPAT, 1988). The Communication Workers of America indicated that about 51,000 of their members are exposed to multiple diisocyanates, including HDI. Of these, about 45,000 telecommunications cable splicers and outside plant technicians work with plugging compounds containing HDI. The remaining 6,000 workers are exposed to diisocyanate-containing inks and RIM plastics (Ref. 5, CWA, 1988).

The civilian and military aircraft industry uses aliphatic diisocyanate-containing paint almost exclusively because of its stability in ultraviolet light (Ref. 8, Hulse, 1984). The number of persons potentially exposed to HDI through these occupations is not known at this time.

In summary, excluding individuals exposed through the aerospace industries and the military, it appears that between 265,000 and 1,315,000 workers are potentially exposed to HDI-containing products.

Between 1978 and 1982, Mobay conducted field industrial hygiene surveys during spray applications of HDI-containing paint systems. Data gathered during six different surveys demonstrated HDI concentrations between <0.005 ppm and 0.04 ppm (Ref. 16, Mobay, 1982). As shown in a section 8(d) submission from Mobay, oven exhaust from a heat-cured urethane resulted in monomeric HDI concentrations of 230 ppb (Ref. 17, Mobay, 1978). This level exceeded the ACGIH threshold limit value (TLV) and NIOSH recommended short-term exposure limit (STEL) of 20 ppb by about 11 times.

A study was conducted to determine the airborne concentrations of total reactive isocyanate groups (-NCOs) from the application of consumer-available polyurethane products. A two-part HDI-containing polyurethane enamel was used in a controlled area simulating a workshop/garage. The product was sprayed on a metal bookcase. Analyses of personal and area air samples collected during the spray application of the enamel found -NCO groups in excess of the upper limit of detection, >5.0 mg NCO/m³ or >2.9 ppm (Ref. 20, MRI, 1987). This level was almost 300 times the NIOSH-recommended 10-minute STEL of 0.02 ppm.

II. Chemical Fate Information

Although HDI is likely to be released to the environment, primarily in fugitive air emissions, it is not expected to persist and should be rapidly

transformed, especially in the presence of liquid water. Therefore, chemical fate testing is not recommended at this time.

III. Biological Effects of Concern to Human Health

A. Metabolism and Toxicokinetics

No information was found.

B. Acute (short-term) Effects

The acute and subacute toxicity of HDI are summarized in the following Tables 3 and 4.

TABLE 3.—CRITICAL END POINTS FOR THE ACUTE/SUBACUTE TOXIC EFFECTS OF HDI

Test	Test subject [a]	Critical toxic effect end points from multiple dose/concentration studies		Reference
		LOEL [b]	NOEL [c]	
Skin irritation	Guinea pig	0.4 mg/animal (approx.)	0.2 mg/animal (approx.)	Kondrat'yev and Mustayev (1969, Ref. 13).
Ocular irritation	Rabbit	NE [d]	NE	Mobay (1961, Ref. 15).
Sensory irritation	Male mouse	0.062 ppm (0.43 mg/m ^{3})	NE	Sangha et al. (1981, Ref. 24).
Pulmonary irritation	Albino rat	NE	NE	Lomonova and Frolova (1968, as cited in NIOSH, 1978, Ref. 22).
Pulmonary irritation	Rabbit	NE	NE	Frolovaya (1966, 1968, as cited in Kondrat'yev and Mustayev 1969, Ref. 13).
Contact sensitivity, induction	Male mouse	8 ug/animal (0.28 mg/kg)	2.1 ug/animal (0.075 mg/kg)	Thorne et al. (1987, Ref. 25).
Contact sensitivity induction	Guinea pig	NE	NE	Kondrat'yev and Mustayev (1969, Ref. 13).
Contact sensitivity elicitation	Guinea pig	8 ug/animal (approx.)	NE	Kondrat'yev and Mustayev (1969, Ref. 13).
Contact sensitivity elicitation	Male mouse	NE	NE	Thorne et al. (1987, Ref. 25).

[a] With the exception of the mice used in the Sangha et al. (1981) study, test animal parameters such as sex, age, weight, and strain were not reported.
[b] Lowest-observable-effects level.
[c] No-observable-effects level.
[d] NE, not established in this study.

TABLE 4.—ACUTE TOXICITY OF HDI IN LABORATORY ANIMALS

Species	LC_{50}		Duration (hours)	LD_{50}		Reference
	Concentration			Oral (mg/kg)	Dermal (mg/kg)	
	(mg/m^3)	(ppm)				
Rat	385	56	6	710		Woolrich (1982, Ref. 28).
Rat (M)	310	45	4			Bunge et al. (1977, as cited in NIOSH, 1978, Ref. 22).
Rat (F)	350	51	4			Bunge et al. (1977, as cited in NIOSH, 1978, Ref. 22).
Rat				1,050		Mobay (1961, Ref. 15).
Mouse	30	4	2			Lomonova and Frolova (1968, as cited in NIOSH, 1978, Ref. 22).
Rabbit					570	Woolrich (1982, Ref. 28).
Rabbit					[a]	Mobay (1961, Ref. 15).

[a] Single dermal doses of 1,000 to 1,250 mg/kg caused lethality, damage to subcutaneous layers of skin, and systemic injury including extensive pulmonary congestion.

HDI is known to produce irritation and inflammation of the upper respiratory tract, so-called sensory irritation. Sangha et al. (Ref. 24, 1981) conducted an acute inhalation study with mice. Depression of the respiratory rate was observed at the lowest dose of HDI tested, 62 ppb (0.43 mg/m ^{3}). No LOEL was established.

Experiments dealing with the elicitation of dermal HDI hypersensitivity were performed early in the study of diisocyanates. A key study with guinea pigs published in 1969 by Kondrat'yev and Mustayev (Ref. 13, 1969) provided a LOEL of 8 ug per animal. Since this is the lowest dose that has been tested in this manner, it is clear that a NOEL has not yet been established.

Thorne et al. (Ref. 25, 1987) induced dermal sensitization to HDI in mice by application of a single dose to shaved abdominal skin. Sensitization was demonstrated by a single challenge does to the ear. The SD^{50} (does predicted to sensitize 50 percent of the animals) upon homologous challenge for HDI was 0.088 mg/kg. The LOEL for HDI was 8 ug per animal; the NOEL was 2.1 ug per animal.

C. Genotoxicity.

In the *Salmonella* assay, HDI was not mutagenic in strains TA100, TA98, or TA1537 with or without metabolic activation. A wide dose range, up to the highest noninhibitory dose, was used (Ref. 3, Andersen et al., 1980). HDI is also reported to inhibit mutagenesis induced by ultraviolet light in an *Escherichia coli* wild-type strain but not in DNA-repair-enzyme deficient strain (Ref. 12, Kawazoe et al., 1981)

D. Oncogenicity

The Mobay Corporation is conducting a 2-year inhalation toxicity/oncogenicity study for HDI. Male and female Fischer 344 rats were exposed to 0, 0.005, 0.025, and 0.125 ppm for 0 to 4 months and to 0.175 ppm thereafter. The exposure regimen was 6 hours per day, 5 days per week for approximately 24 months.

Sixty rats of each sex were exposed at each level, and 10 rats of each sex at each level for a satellite group. Preliminary review of the data indicated no toxicologically significant effects on body weight, ophthalmology or mortality; no other parameters were evaluated. The final report is scheduled to be completed during mid-1989 (Ref. 18, Mobay, 1988a).

E. Chronic (Long-term) Effects

No information was found.

F. Reproductive and Developmental Effects

No information was found.

G. Observations in Humans

Allegations of adverse health effects following exposure to HDI (and other diisocyanates) were the subject of a TSCA section 8(c) reporting rule (53 FR 1408; January 19, 1988). The rule required only submission of unknown or unreported adverse health effects. Several of these involved a two-part polyurethane enamel. The activator for this enamel contains over 70 percent HDI-polyisocyanate. According to the Material Safety Data Sheet, HDI monomer is controlled to <0.7 percent by weight. With aging, the monomer content may increase to 1.6 percent by weight (Ref. 6, Dupont, 1981.)

One case study describes an individual who inadvertently stepped into a puddle of two-part polyurethane enamel. This person began to experience immediate "trouble", which gradually worsened to a burning sensation up to mid thigh with aching discomfort and mild weakness in foot muscles. Another case associated exposure to the two-part polyurethane enamel with subsequent testicular cancer and terminal chest cancer. A third case involved 12 men employed in an unspecified job; all experienced urological problems allegedly due to exposure to this enamel (Ref. 7, Dupont, 1988).

Another reported incident involved firefighters exposed to the two-part polyurethane enamel. This paint was used in firehouses in Balitmore, MD between January 1982 and March 1984. Of 10 infants fathered during this 15-month interval, 8 died during spontaneous abortion or soon after birth. A similar report involved a man employed in an autobody shop and exposed to this enamel. He claimed that his exposure prior to and subsequent to the conception of his son was responsible for severe birth defects (Ref. 7, Dupont, 1988).

Many case-specific reports suggest adverse health effects following exposure to polymeric HDI. Of particular note is a case described by Malo et al. (1983, as cited in Karol, 1987, Ref. 11), in which an individual exposed to a spray paint containing polymeric HDI experienced shortness of breath, wheezing, malaise, and chills late in the afternoon on working days. Symptoms lasted for several hours and were accompanied by wheezing at night. Inhalation challenge under simulated occupational exposure conditions reproduced the symptoms and thereby identified the source of the active material.

A recently published study of Swedish car painters exposed both to HDI and biuret-modified HDI at average concentrations of 0.001 ppm and 0.013 ppm, respectively, demonstrated that pulmonary closing volume was increased in car painters relative to vita capacity; controls did not exhibit this decrement. The authors found this suggestive of "small airways disease" (Ref. 2, Alexandersson et al., 1987).

H. Rationale for Health Effects Recommendations.

Annual domestic production of HDI is about 11 million pounds. It is estimated that well over 1 million individuals are exposed to this chemical in the workplace, as a result of its use in coatings. Although one carcinogenicity study is currently being conducted in one rodent species, data are not available to assess fully the long-term effects of HDI. Therefore, the Committee recommends that chronic toxicity studies with carcinogenicity as an endpoint be conducted in another species in accordance with accepted guidelines for carcinogenicity testing. The Committee also is concerned about available human data suggesting potential reproductive impairment. Considering the lack of definitive reproductive and developmental effects data, the Commitee recommends that testing addressing these specific endpoints also be conducted.

IV. Ecological Effects of Concern

Since HDI is not expected to persist following release to the environment and should be rapidly transformed in the presence of water, ecological effects testing is not being recommended at this time.

References

(1) ACGIH. "Threshold Limit Values for Chemical and Physical Agents, 1976," Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

(2) Alexandersson, R., Plato, N., Hedenstierna, G., Kolmodin-Hedman, B. "Exposure, lung function, and symptoms in car painters exposed to hexamethylene-diisocyanate and biuret modified hexamethylene-diisocyanate," *Archives of Environmental Health.* 42:367–373 (1987).

(3) Andersen, M., Binderup, M.L., Kiel, P., Larsen, H. and Maxild, J. "Mutagenic action of isocyanates used in the production of polyurethanes," *Scandinavian Journal Work Environmental Health.* 6:221–226 (1980).

(4) ASA. Personal communication from J. Caldwell, former Executive Secretary, Automotive Services Association (ASA), Laguna, CA, to S. Strassman-Sundy, Risk Analysis Branch, Office of Toxic Substances, U.S. Environmental Protection Agency (March 14, 1988).

(5) CWA. Letter from D. LeGrande, Occupational Safety and Health Coordinator, Communication Workers of America (CWA), Washington, DC, to S. Strassman-Sundy, Risk Analysis Branch, Office of Toxic Substances, U.S. Environmental Protection Agency (March 31, 1988).

(6) DuPont. Material Safety Data Sheet on 192S Activator. E.I. du Pont de Nemours & Co., Inc. (1981).

(7) DuPont. Section 8(c) submission number 8CL-0388-0002; E.I. du Pont de Nemours & Co., Inc. (March 4, 1988).

(8) Hulse, P.M. "An evaluation of HDI in polyurethane spray paint aerosols," Masters Thesis. The John Hopkins University, Division of Environmental Health Engineering, School of Hygiene & Public Health, Baltimore, MD (1984).

(9) IBPAT. Personal communication from R. Wolford, Health and Safety Officer, International Brotherhood of Painters and Allied Trades (IBPAT), Washington, DC, to S. Strassman-Sundy, Risk Analysis Branch, Office of Toxic Substances, U.S. Environmental Protection Agency (March 22, 1988).

(10) ICF. "Producers and Users of Diisocyanates," Washington, DC: ICF Incorporated, U.S. EPA Contract No. 68-02-3976; Work Assignment No. 1-25 (June 30, 1986).

(11) Karol, M.H. "Respiratory effects of inhaled isocyanates," *CRC Critical Reviews in Toxicology.* 16(4):349–379 (1987).

(12) Kawazoe, Y., Kato, M., and Takahashi, K. "Studies on chemical carcinogens. XX. Inhibitory effect of alkyl isocyanates and isothiocyanates on mutagenesis in *E. coli* by ultraviolet radiation," *Chemical and Pharmaceutical Bulletin.* 29:2631–2638 (1981).

(13) Kondrat'yev, G.G., Mustayev, R.K. "Study of the allergic properties of hexamethylene-diisocyanate in an experiment," (Rus.) *Gigiyena Primeneniya Polimernykh Materialov i Izdeliy Iz Nikh.*, Nr. 1, pp. 290–293. Translated by: Translation

Division. Foreign Technology Division. Wright Patterson AFB, Ohio (1969).
(14) Leo, A.R., Hansch, C., and Elkins, D. "Partition coefficients and their uses," *Chemical Reviews.* 71(6):525–615 (1971).
(15) Mobay. "Toxicity and Safe Handling of Isocyanates. A Review of the Literature (TDI) and Results of Toxicity Screening Studies on Additional Compounds," Pittsburgh, PA: Mobay Chemical Company (1961).
(16) Mobay. Letter from C.L.H. Howard, Vice President-Scientific, Mobay Chemical Corporation to M. Greif, TSCA Interagency Testing Committee (July 20, 1982).
(17) Mobay. TSCA Section 8(d) submission number 86–870001276; Mobay Corporation (July 29, 1987).
(18) Mobay. Letter from Francis J. Rattay, Manager, Regulatory Compliance, Mobay Corporation, Pittsburgh, PA, to Robert Brink, TSCA Interagency Testing Committee (January 21, 1988a).
(19) Mobay. Personal communication from F.J. Rattay, Manager, Regulatory Compliance, Mobay Corporation, Pittsburgh, PA, to R. Wedge, Dynamac Corporation (March 14, 1988b).
(20) MRI. Total Isocyanates—ACE Laboratory Experiment. Kansas City, MI: Midwest Research Institute. U.S. EPA Contract 68–02–4252; Work Assignment No. 51 (October 29, 1987).
(21) NIOSH. National Occupational Hazard Survey (1972–1974) [data base]. Cincinnati, OH: National Institute for Occupational Safety and Health, Department of Health and Human Services (1976).
(22) NIOSH. "Criteria for a recommended standard occupational exposure to diisocyanates," Rockville MD: National Institute for Occupational Safety and Health. NIOSH–78–215. PB81–226615 (1978).
(23) NIOSH. National Occupational Exposure Survey (1980–1983) [data base]. Cincinnati, OH: National Institute for Occupational Safety and Health, Department of Health and Human Services (1984).
(24) Sangha, G.K., Matijak, M., Alarie, Y. "Comparison of some mono- and diisocyanates as sensory irritants," *Toxicology and Applied Pharmacology.* 57:241–246 (1981).
(25) Thorne, P.S., Hillebrand, J.A., Lewis, G.R., Karol, M.H. "Contact sensitivity by diisocyanates: Potencies and cross-reactivities," *Toxicology and Applied Pharmacology.* 87:155–165 (1987).
(26) UAW. Personal communication from F. Mirer, Health and Safety Director, United Auto Workers, Detroit, MI, to L. Borghi, Dynamac Corporation (March 16, 1988).
(27) USEPA. TSCA Chemical Substance Inventory (non-confidential) [data base]. Washington, DC: U.S. Environmental Protection Agency (1988).
(28) Woolrich, P.F. "Toxicology, industrial hygiene and medical control of TDI, MDI, and PMPPI," *American Industrial Hygiene Journal.* 43:89–97 (1982).

2.3 *Chemicals recommended with intent-to-designate—2.3a Crotonaldehyde—Summary of recommended studies.* It is recommended that crotonaldehyde be tested for the following:

1. *Chemical fate:* Volatilization rate from water. Aerobic aquatic biodegradation rate.
2. *Health effects:* None.
3. *Ecological effects:* Acute toxicity to algae, fish, and aquatic invertebrates.

Physical and Chemical Information

CAS Number: 4170–30–3
Synonyms: 2–Butenal (9 CI); B–Methyl acrolein; Crotonal; Crotonic aldehyde; Propylene aldehyde.
Structural Formula:

$$CH_3CH{=}CHCHO$$

Empirical Formula: C_4H_6O
Molecular Weight: 70.1
Melting Point: -76.5°C (Ref. 6, Merck, 1983); -69°C (Ref. 8, Sax and Lewis, 1987)
Boiling Point: 104.0°C (Ref. 6, Merck, 1983); 102°C (Ref. 8, Sax and Lewis, 1987)
Vapor Pressure: 30 mmHg at 20°C (Ref. 8, Sax and Lewis, 1987); 19 mmHg at 20°C (Ref. 11, Verschueren, 1983)
Solubility in Water: 155 g/L at 20°C (Ref. 11, Verschueren, 1983); 18.1 g/100 g at 20°C (Ref. 6, Merck, 1983)
Specific Gravity: 0.853 at 20/20°C (Ref. 6, Merck, 1983)
Log Octanol/Water Partition Coefficient (log P): 0.55 (Est'd; Ref. 7, NRC, 1981)
Henry's Law Constant: 1.7×10^{-5} atm m^3/mole, calculated
Description of Chemical: Water white, mobile liquid with a pungent, suffocating odor (Ref. 8, Sax and Lewis, 1987)

Rationale for Recommendation

I. Exposure Information

A. *Production/Use/Release to Environment*

Most crotonaldehyde is manufactured from acetaldehyde using continuous, enclosed reactor systems via the aldol condensation route, although a variety of less common methods may be used (Ref. 4, Kirk-Othmer, 1979). Annual current and projected U.S. production is from 5 to 15 million pounds (Ref. 2, Eastman Kodak, 1987). Crotonaldehyde also may be formed naturally in the atmosphere by the interaction of reactive molecules such as ozone and hydroxyl radicals with hydrocarbons and their oxidation products (Ref. 7, NRC, 1981). Crotonaldehyde is used primarily as a chemical intermediate for the synthesis of other organic compounds such as n-butanol, sorbic acid, 3-methoxybutanal, and crotonic acid (Ref. 4, Kirk-Othmer, 1979).

Releases of crotonaldehyde to the environment are expected to occur in wastewater.

B. *Evidence for Exposure*

Crotonaldehyde has been detected in the effluent of sewage treatment plants (Ref. 9, Shackelford and Keith, 1976). Exhaust from cars without emission controls was found to contain crotonaldehyde (Ref. 7, NRC, 1981). Crotonaldehyde also has been identified as a constituent of tobacco smoke (Ref. 3, Florin et al., 1980) and wood smoke (Ref. 5, Lipari et al., 1984).

II. Chemical Fate Information

A. *Transport*

Environmental releases are expected to be from wastewater. The physical and chemical properties of crotonaldehyde indicate that it will partition to both air and water following release to the environment. The Henry's Law Constant of 1.7×10^{-5} atm m^3/mole allows an estimation of the half-life in receiving stream water of 60 to 70 hours. Sorption to solids will not be significant.

B. *Persistence*

Crotonaldehyde released directly to the atmosphere or evaporated from surface water will be rapidly degraded by reactions with hydroxyl radicals and ozone and by direct sunlight photolysis. Biodegradation is expected to be the most significant transformation process in water, but no aquatic biodegradation rate data were found. The 5-day biochemical oxygen demand (BOD) for crotonaldehyde was reported as 37 percent of theory (Ref. 11, Verschueren, 1983) and 51 percent of theory (Ref. 10, Union Carbide, 1986). The Union Carbide reference also lists BOD data after 10, 15, and 20 days incubation as 60 percent, 64 percent and 70 percent of theory, respectively. These data suggest ready and complete biodegradation when sewage or sludge, which may be acclimated to crotonaldehyde, are used as the inoculum, but they do not permit a determination of the biodegradation half-life in receiving systems.

C. *Rationale for Chemical Fate Recommendation*

Since crotonaldehyde may be released to surface waters at manufacturing and use sites, it is necessary to obtain experimental data on volatilization rates from water and on the aerobic, aquatic biodegradation rate to better assess potential environmental concentrations.

III. Biological Effects of Concern to Human Health

The Committee determined that crotonaldehyde has been studied extensively for health effects and concluded that additional studies are not required. Therefore, health effects testing is not being recommended at this time.

IV. Ecological Effects of Concern

A. *Acute and Subchronic (Short-term) Effects*

An 85 percent aqueous solution of crotonaldehyde produced a 96-hour LC_{50} of 3.5 mg/L to bluegills (*Lepomis macrochirus*) in a static bioassay at 20° C (Ref. 1, Dawson et al., 1977). A 96-hour LC_{50} value of 2.8 mg/L with fathead minnows (*Pimephales promelas*) was reported by Union Carbide (Ref. 10, 1986). The 96-hour LC_{50} for tidewater silversides (*Menidia beryllina*) was reported to be 1.3 mg/L in a static bioassay at 20° C (Ref. 1, Dawson et al. 1977). Percent survival of silversides decreased with exposure time.

B. *Chronic (long-term) Effects*

No information was found.

C. *Other Ecological Effects*

Sewage treatment microorganisms were reported to be adversely affected by 25 to 50 mg/L crotonaldehyde (Ref. 10, Union Carbide, 1986). At concentrations from 0.05 to 1.0 percent, crotonaldehyde produced an immediate loss of the metachronic wave in the lateral cilia of freshwater mussels (*Lamellibranchiata unio*) (Ref. 12, Wynder et al., 1965). At the 0.5 and 1.0 percent concentrations, total stasis in mussel cilia was observed, with no recovery.

D. *Bioconcentration and Food-Chain Transport*

No information was found, but the high water solubility and low log P of crotonaldehyde make it unlikely that any sigificant bioconcentration will occur.

E. *Rationale for Ecological Effects Recommendation*

The available data, from tests using nominal concentrations in static tests, show that crotonaldehyde has significant acute toxicity to both freshwater and marine fish. It is necessary to develop more reliable acute toxicity data using measured concentrations of crotonaldehyde in flow-through or static-renewal tests, using algae, fish, and aquatic invertebrates.

References

(1) Dawson, G.W., Jennings, A.L. Drozdowski, D., Rider, E. "The acute toxicity of 47 industrial chemicals to fresh and saltwater fishes," *Journal of Hazardous Materials*. 1:303–318 (1977).

(2) Eastman Kodak. Letter from R.D. Gerwe, Senior Product Safety Representative, Eastman Kodak Co., Kingsport, TN to R.H. Brink, TSCA Interagency Testing Committee (June 19, 1987).

(3) Florin, I., Rutberg, L., Curvall, M., and Enzell, C.R. "Screening of tobacco smoke constituents for mutagenicity using the Ames' test," *Toxicology*. 18:219–232 (1980).

(4) Kirk-Othmer. *Kirk-Othmer Encyclopedia of Chemical Technology*. New York, NY: John Wiley & Sons, Inc. Vol. 7, pp. 207–218 (1979).

(5) Lipari, F., Dasch, J.M., Scruggs, W.F. "Aldehyde emissions from wood-burning fireplaces," *Environmental Science and Technology*. 18(5):326–330 (1984).

(6) Merck. *The Merck Index*. 10th Ed. Windholz, M., ed. Rahway, NJ: Merck & Company. p. 372 (1983).

(7) NRC. National Research Council. *Formaldehyde and Other Aldehydes*. Washington, DC: National Academy Press (1981).

(8) Sax, N.I. and Lewis, R.J., Sr. *Hawley's Condensed Chemical Dictionary*. 11th Rev. Ed. New York, NY: Van Nostrand Reinhold Co. p. 323 (1987).

(9) Shackelford, W.M., Keith, L.H. "Frequency of organic compounds identified in water," Athens, GA: U.S. Environmental Protection Agency, Environmental Research Laboratory. EPA Report No. EPA-600/4-76-062. p. 102 (1976).

(10) Union Carbide. Letter from D.L. Heywood, Assistant Director, Product Safety, Union Carbide Corp., Danbury, CT to U.S. Environmental Protection Agency (May 2, 1986).

(11) Verschueren, K. *Handbook of Environmental Data on Organic Chemicals*. 2nd Ed. New York, NY: Van Nostrand Reinhold Co. pp. 410–411 (1983).

(12) Wynder, E.L., Goodman, D.A., Hoffmann, D. "Ciliatoxic components in cigarette smoke. II. Carboxylic acids and aldehydes," *Cancer*. 18(4):505–509 (1965).

2.4. *Chemicals recommended without being designated for response within 12 months—2.4.a Imidazolium quaternary ammonium compounds—Summary of recommended studies.* It is recommended that the imidazolium quaternary ammonium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl), methyl sulfates (IQAC) be tested for the following:

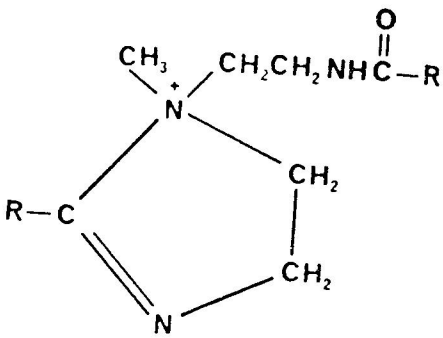
1. *Chemical fate:* Aerobic and anaerobic biodegradation of IQAC sorbed to freshwater and estuarine sediments.

2. *Health effects:* Chronic toxicity studies to evaluate potential effects through long-term dermal exposure.

3. *Ecological effects:* Acute and chronic studies to evaluate effects on representative freshwater and estuarine benthic organisms.

Physical and Chemical Information

CAS Number: 68122–86–1
9 CI Name: Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl), Me sulfates
Synonym: Imidazolium quaternary ammonium compounds
Acronym: IQAC
Structural Formula:



where R = tallow
Empirical Formula (typically): $C_{37}H_{74}N_3O$ to $C_{41}H_{82}N_3O$
Molecular Weight: 577.0 for $R = C_{15}H_{31}$; 633.1 for $R = C_{17}H_{35}$
Boiling Point: ≤260°C (Ref. 3, Capital City Products, 1986)
Solubility in Water: 19.2 mg/L in deionized water after 16 days of continuous mixing; 0.5 mg/L in filtered river water after 16 days of continuous mixing (Ref. 4, Procter and Gamble, 1984a)
Specific Gravity: No information was found.
Log Octanol/Water Partition Coefficient (log P): 2.15, measured (Ref. 4, Proter and Gamble, 1984a)

Rationale for Recommendations

I. Exposure Information

A. Production/Use/Release to Environment

IQAC production in 1984 was estimated at about 15 million pounds in the U.S. (Ref., 4, Procter and Gamble, 1984a). The TSCA Inventory update contains confidential 1986 production information for IQAC. The major use of IQAC appears to be in fabric softeners used during the clothes-washing process. Analogs of IQAC that might also be used in fabric softener formulations include chemical mixtures with the following CAS Nos.: 68132–27–4, 69011–82–1, 70775–90–5, 71060–67–8, 71060–68–9, 72275–90–2, 72623–81–5 and 72623–82–6. If these compounds or

similar imidazolium quaternary ammonium compounds are used now, or in the future, in substantial quantities as ingredients in fabric softeners for consumer use, the Committee would have the same environmental fate, health effects and ecological effects concerns for them as for IQAC. IQAC and any of its analogs used in fabric softeners are likely to be released to the environment in wastewater following their use.

B. Evidence for Exposure

General population exposure to IQAC may be high given its use in fabric softeners used in laundry washing machines. Consumers who use this type of fabric softener are likely to be exposed almost continuously through skin contact with clothing, towels and linens. An assessment by the Office of Toxic Substances (Ref. 1, Battin, 1988a) estimated annual consumer dermal exposure to IQAC, from exposure to softened clothing, linens, etc., at 4.06 to 10.14 g per year. Procter and Gamble (Ref. 4, 1984a) estimated daily consumer exposure to IQAC, from clothing to skin, to be 0.07 mg active compound per kg per day for adults and 0.14 mg active compound per kg per day for children assuming IQAC is deposited on fabrics at 0.17 mg/in^2. No environmental monitoring studies were found. An assessment by the Office of Toxic Substances (Ref. 1, Battin, 1988a) estimated receiving stream concentrations of 1 to 1,300 ug/L at manufacturing sites and 0.05 to 50 ug/L near use sites, depending upon location and stream flows. Procter and Gamble (Ref. 4, 1984a) estimated that consumer use of IQAC would yield raw wastewater concentrations of about 170 ug/L.

II. Chemical Fate Information

A. Transport

The physical and chemical properties of IQAC indicate that it will partition significantly to sludge solids and sediments with some remaining dissolved in water. The estimated very low vapor pressure and moderate solubility rule out volatilization as an important factor. The cationic nature of these compounds will contribute to their sorption to sludge and sediment solids which generally are negatively charged and it is expected that IQAC will sorb to solids within a short time after release to the environment.

B. Persistence

No published information was found on the persistence of IQAC. A summary report of an unpublished study (Ref. 4, Procter and Gamble, 1984a) showed about 50 percent biodegradation in 34 days in diluted activated sludge, as determined by following the evolution of radiolabelled carbon dixoide. The concentration of IQAC was not reported. BOD studies reported by Sherex (Ref. 6, 1984) showed 2 percent of theoretical oxygen uptake after 5 days and 19 percent after 30 days. While this indicates that IQAC is biodegradable under aerobic conditions, it also indicates that biodegradation in surface waters is likely to be slow. IQAC is expected to partition significantly to sediments following release to the environment and its persistence in sediments, under both aerobic and anaerobic conditions, is unknown. Also unknown is the persistence of IQAC under conditions found in estuaries and the ocean. Persistence in saline waters may be different than in fresh water. Nitrilotriacetic acid, for example, was found to be resistant to biodegradation in estuarine waters (Ref. 2, Bourquin and Przybyszewski, 1977) although it is readily biodegraded by acclimated microorganisms in fresh water.

C. *Rationale for Chemical Fate Recommendations*

IQAC is likely to sorb strongly to waste treatment sludges and receiving stream organic sediments and may persist for relatively long time periods following sorption. Since it is being released continuously to both fresh water and estuarine receiving waters and may persist for relatively long periods of time, there may be a tendency for it to accumulate in estuarine, river and lake sediments near discharge points, with gradually increasing concentrations. There is a need to better determine the persistence of IQAC, dissolved in water and sorbed to sediments. It is recommended that those studies be conducted under conditions typical of both fresh surface waters and estuarine waters and that studies with IQAC sorbed to sediment be conducted under both aerobic and anaerobic conditions. Information from these studies is needed to better assess the potential concentration of IQAC in receiving waters and sediment and the potential hazard to aquatic and benthic organisms.

III. Biological Effects of Concern to Human Health

A. *Metabolism and Toxicokinetics*

A summary of metabolism studies (Ref. 4, Procter and Gamble, 1984a) using radiolabelled IQAC (^{14}C on the N-methyl group) suggests that the compound is poorly absorbed in rats via both oral and dermal routes. Upon oral administration, less than 1 percent of the oral dose was absorbed and metabolized. Eighty-seven percent of the oral dose was eliminated in feces within 24 hours. A "small but significant amount of radioactivity was found in the bone marrow" (Ref. 4, Procter and Gamble, 1948a). Less than 0.5 percent of the dermal dose was absorbed, with a small amount of radioactivity found in the bone marrow.

B. *Acute and Subchronic (Short-term) Effects.*

Summary reports on unpublished data from acute oral, dermal skin irritation, eye irritation, skin sensitization, and subchronic toxicity studies with IQAC were submitted by Procter and Gamble (Ref. 4, 1984a and Ref. 5, 1988). Data from acute oral, skin and eye irritation, and skin sensitization studies were submitted by Sherex (Ref. 6, 1984). Acute oral tests with IQAC in rats yielded an LD_{50} of 20.8 g/kg in one test (Ref. 6, Sherex, 1984) and 2 deaths out of 10 in another test at a dose level of about 18 g active compound per kg (Ref. 4, Procter and Gamble, 1984a). In another study, no deaths were reported with oral doses up to 16 cc of IQAC dispersion (13.5 wt percent solid) per kg (Ref. 6, Sherex, 1984).

Procter and Gamble reported moderate to severe irritation for IQAC instilled into the conjunctival sac of rabbit eyes unrinsed after treatment (Ref. 4, 1984a). However, it produced minimal irritation to rinsed rabbit eyes (Ref. 4, Procter and Gamble, 1984a; Ref. 6, Sherex, 1984).

Percutaneous studies with IQAC in rabbits yielded a minimum lethal dose of greater than 1.8 g active compound per kg (Ref. 4, Procter and Gamble, 1984a).

Primary skin irritation studies conducted with IQAC on intact and abraded rabbit skin indicated moderate to severe irritation in one study (Ref. 4, Procter and Gamble, 1984a) and only mild irritation in another (Ref. 6, Sherex, 1984).

Skin sensitization studies with IQAC by Procter and Gamble (Ref. 4, 1984a) showed delayed contact hypersensitivity in 17 out of 20 guinea pigs tested. Sherex (Ref. 6, 1984), on the other hand, reported that IQAC was not a strong sensitizer in guinea pigs tested with three different lots.

In a subchronic toxicity study (Ref. 4, Procter and Gamble, 1984a) four groups of 20 male and 20 female rats each were fed a diet containing IQAC at concentrations of 0, 10, 100, or 1,000 mg

active compound per kg per day for 13 weeks. There were no treatment-related changes in mean body weights or food consumption. Lower total protein and higher serum glutamic-pyruvic transaminase values were observed in blood samples of males in the 1,000 mg per kg group. These males also showed lower absolute and relative liver weights. No treatment-related changes were observed in bone marrow. The no-observable-effects level (NOEL) was 100 mg per kg per day. According to Procter and Gamble, this level is at least 10 million times the expected daily human exposure to IQAC in drinking water.

In a percutaneous subchronic toxicity test, two groups of 5 male and 5 female rabbits each were treated topically with 2 mL per kg per day IQAC at dose levels of 3 or 27 mg active compound per kg per day for 13 weeks (Ref. 4, Procter and Gamble, 1984a). A control group of 5 males and 5 females received the vehicle, distilled water. Slight to moderate erythema, edema, and desquamation were observed in treated animals at both doses. No treatment-related changes were observed in clinical pathology, bone marrow smears, body weights, organ weights, microscopic changes in skin, or histopathologic changes to internal organs. The NOEL for systemic toxicity was 27 mg active compound kg per day.

C. *Genotoxicity*

IQAC was tested for mutagenicity in the *Salmonella* assay (with and without metabolic activation), mouse lymphoma assay, rat *in vitro* cytogenetics assay, and for unscheduled DNA synthesis in human diploid cells (Ref. 4, Procter and Gamble, 1984a). IQAC did not show mutagenic effects in any of the assays.

D. Oncogenicity

No information was found.

E. Reproductive and Developmental Effects

Rats were administered IQAC (78 percent active compound) by gavage at dose levels of 200 or 600 mg active compound per kg daily from days 6 to 12 or 15 of gestation (Ref. 4, Procter and Gamble, 1984a). A control group received the vehicle, 15 percent w/v aqueous isopropanol. Doses were given to each group of 30 females at a constant volume of 2 mL per kg per day. The animals were observed for mortality, clinical signs, body weight changes, and food consumption. No maternal deaths were observed. A decrease in food consumption was found in the 600 mg per kg per day group during the first 3 days. Overall reproduction parameters and pregnancy rates were unaffected. The incidences of skeletal and soft-tissue defects were not significantly different between the treated and the control groups. At the highest dose tested (600 mg active compound per kg per day) no maternal or developmental toxicity was observed.

F. Chronic (Long-term) Effects

No information was found.

G. Observations in Humans

Little or no irritation was observed with human volunteers in a skin irritation test with a dilute, aqueous dispersion of 0.3 mL IQAC per occluded patch (Ref. 4, Procter and Gamble, 1984a). IQAC was tested in three 24-hour exposures over a 6-day period at concentrations of 0.5, 1.0, and 5.0 percent w/v. In another Procter and Gamble study (Ref. 4, 1984a), 217 volunteers received 9 exposures to 0.25 percent w/v aqueous IQAC (0.3 mL per occluded patch) applied for a 24-hour period, 3 times a week during a 3-week induction period. No skin sensitization was observed when subjects were challenged 2 weeks later with 0.25 percent w/v IQAC in a single 24-hour occluded patch test.

H. Rationale for Health Effects Recommendations

It has been estimated that fabric softeners that are applied to the fabrics during the washing process are widely used in the U.S. Annual U.S. consumption of imidazolium quaternary ammonium type fabric softeners has been estimated at about 15 million pounds. It is quite apparent that a significant portion of the population is exposed, on a nearly continuous basis, to these chemicals in clothing, towels and bed linens. Dermal exposure tests reported to date have involved only acute or short-term exposures. IQAC produced moderate to severe skin irritation in rabbits and was a skin sensitizer in guinea pigs.

Although exposure concentrations used in short-term studies were reported to be several-fold higher than estimated human exposures from softened fabrics, information from these short-term, intermittent-exposure tests is not useful in predicting what effects might occur with long-term (years) continuous exposure. It is therefore recommended that IQAC and commercially important analogs be tested for chronic toxicity to evaluate potential effects resulting from long-term dermal exposure.

IV. Ecological Effects of Concern

A. Acute and Subchronic (Short-term) Effects

Data submitted by Procter and Gamble (Ref. 4, 1984a) show moderate toxicity to bluegills, mysid shrimp and *Daphnia magna*. The presence of anionic surfactants or the use of natural surface water with sediments mitigated the effects on bluegills and daphnia. No data were found for benthic organisms and this is a data gap of concern since IQAC will sorb to and may concentrate in sediments near wastewater discharge sites.

B. Chronic (Long-term) Effects

No published information was found but Procter and Gamble (Ref. 5, 1988) indicated that data have been developed with a hydrogenated analog of IQAC in chronic studies with midge.

C. Other Ecological Effects (Biological, Behavioral, or Ecosystem Processes)

IQAC was reported (Ref. 4, Procter and Gamble, 1984a) to inhibit algal growth at relatively low concentrations. The algistatic concentrations were 0.037 mg/L for a *Selenastrum* sp. and 0.23 mg/L for a *Microcystis* sp.

D. Bioconcentration and Food-chain Transport

The measured log P of 2.15 indicates a potential for some bioconcentration. Procter and Gamble (Ref. 4, 1984a) reported a measured bioconcentration factor (BCF) of 10.7 for bluegills exposed to 8.8 g/L IQAC in a flow-through system. This report is suspect because the reported concentration of IQAC is well above its water solubility. Nevertheless, the evidence is that there may be some bioconcentration.

E. Rationale for Ecological Effects Recommendations

Environmental fate considerations indicated that IQAC will sorb strongly to sludge solids and sediments. It may persist for relatively long time periods under these conditions and may accumulate in sediments near wastewater discharges. This information plus the known toxicity of IQAC to fish, aquatic invertebrates and algae, raise concerns for benthic organisms. Acute toxicity data should be obtained for representative freshwater and estuarine benthic organisms and, if these compounds are found to be relatively persistent, chronic studies on the same organisms may be warranted.

References

(1) Battin, A. Memorandum on exposure and release of imidazolium quaternary ammonium compounds in liquid fabric softeners from Andrew Battin, Exposure Assessment Branch, Office of Toxic Substances, U.S. Environmental Protection Agency, to John D. Walker, Test Rules Development Branch. (February 2, 1988a.)

(2) Bourquin, A.W. and Przybyszewski, V.A. "Distribution of bacteria and nitrilotriacetate-degrading potential in an estuarine environment." *Applied and Environmental Microbiology.* 34:411–418 (1977).

(3) Capital City Products. Material Safety Data Sheet on Accosoft 808 75 and product literature submitted by Capital City Products, Janesville, WI (November 12, 1986).

(4) Procter and Gamble. Letter from T.W. Mooney, Manager, Technical Government Relations, The Procter and Gamble Co., Cincinnati, OH, to Arthur Stern, TSCA Interagency Testing Committee. (September 12, 1984a.)

(5) Procter and Gamble. Letter from R.N. Sturm, Associate Director, Bar Soap & Household Cleaning Product Development, Procter and Gamble Co., Cincinnati, OH, to Robert Brink, TSCA Interagency Testing Committee (April 19, 1988).

(6) Sherex. Letter from Howard H. Hickman, Manager of Regulatory Affairs, Sherex Chemical Co., Dublin, OH, to Martin Greif, TSCA Interagency Testing Committee. (January 17, 1984.)

2.4.b *Ethoxylated quaternary ammonium compounds—Summary of recommended studies.* It is recommended that ethoxylated quaternary ammonium compounds, EEQ (CAS No. 68153–35–5) and PEQ (CAS No. 68410–69–5) and any commercially important analogs of PEQ (e.g., CAS Nos. 68389–88–8, 68389–89–9, 68413–04–7, 68554–06–3 and 70914–06–3) be tested for the following:

1. *Chemical fate:* Aerobic and anaerobic biodegradation of the ethoxylated quaternary ammonium compounds sorbed to freshwater and estuarine sediments.

2. *Health effects:* Chronic toxicity studies to evaluate potential effects through long-term dermal exposure.

3. *Ecological effects:* Acute and chronic effects on representative freshwater and estuarine benthic organisms.

Physical and Chemical Information

CAS No.: 68153–35–5

9 CI Name: Ethanaminium, 2-amino-N-(2-aminoethyl)-N-(2-hydroxyethyl)-N-methyl-, N,N'-ditallow acyl derivs., Me sulfates (salts)

Synonyms:

Ethoxylated ethanaminium quaternary ammonium compounds;

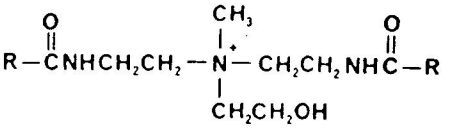
N,N-Bis(2-tallow amidoethyl)-N-(2-hydroxyethyl)-N-methylammonium methyl sulfate;

N,N-Di(2-tallow amidoethyl)-N-(2-hydroxyethyl)-N-methylammonium methyl sulfate;

Quaternary ammonium compounds, (hydroxyethyl)-methylbis(2-tallow amidoethyl), Me sulfates

Acronym: EEQ

Structural Formula:



where R = tallow

Empirical Formula (typically): $C_{39}H_{80}N_3O_3$ to $C_{43}H_{88}N_3O_3$

Molecular Weight:

639.1 where R = $C_{15}H_{31}$

695.5 where R = $C_{17}H_{35}$

Melting Point: 170°C, estimated (Ref. 2, Battin, 1988c)

Boiling Point: 567°C, estimated (Ref. 2, Battin, 1988c)

Vapor Pressure: 2.86×10^{-7} mmHg at 25°C, estimated (Ref. 2, Battin, 1988c)

Solubility in Water: 35 mg/L in deionized water after 14 days of continuous mixing (Ref. 5, Procter and Gamble, 1984b)

Specific Gravity: No information was found.

Log Octanol/Water Partition Coefficient (log P): 2.48, measured (Ref. 5, Proctor and Gamble, 1984b)

Henry's Law Constant: 7.71×10^{-19} atm m^3/mole, estimated (Ref. 2, Battin, 1988c)

Log Adsorption Coefficient (log K_{oc})≤ 2.27, estimated (Ref. 2, Battin, 1988c)

Physical and Chemical Information

CAS No.: 68410–69–5

9 CI Name: Poly(oxy-1,2-ethanediyl), α-[2-[bis(2-aminoethyl)methylammonio]-ethyl]-ω-hydroxy-, N,N-ditallow acyl derivs., Me sulfates (salts)

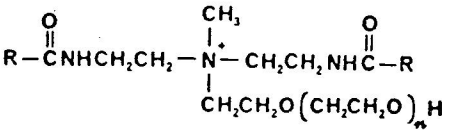
Synonyms:

Methyl tallow diethylenetriamine condensate, polyethoxylated, methyl sulfate;

Quaternary ammonium compounds, (2-hydroxyethyl) methylbis(2-tallow amidoethyl), Me sulfates, ethoxylated

Acronym: PEQ

Structural Formula:



where R = tallow and n = 1–7

Empirical Formula (typically): $C_{41}H_{84}N_3O_4$ to $C_{57}H_{116}N_3O_{10}$

Molecular Weight:

683.2 where R = $C_{15}H_{31}$ and n = 1

1,003.9 where R = $C_{17}H_{35}$ and n = 7

Melting Point: No information was found.

Boiling Point: No information was found.

Vapor Pressure: No information was found.

Solubility in Water: No information was found.

Solubility in Organic Solvents: No information was found.

Specific Gravity: No information was found.

Log Octanol/Water Partition Coefficient (log P): No information was found.

Henry's Law Constant: No information was found.

Log Adsorption Coefficient (log Koc): No information was found.

Rationale for Recommendations

I. Exposure Information

A. Production/Use/Environmental Release

It was estimated that the market for EEQ in 1984 was about 25 million pounds per year in the U.S. (Ref. 5, Procter and Gamble, 1984b). Information obtained during the ITC review of these chemicals indicated that in recent years PEQ has taken a large share of the market away from EEQ. TSCA Inventory update information contains a total for 1986 production and import of EEQ that is classified as confidential business information (CBI). Production and import of PEQ was not reported for the TSCA Inventory update. The lack of PEQ data in the updated Inventory contrasts with reports (to Dynamac Corp.) from industry of substantial current PEQ production. The Committee is unable to obtain current production and import data for PEQ and its analogs because they are classified as polymers and are exempt from Inventory update reporting. However, because of the potential for widespread chronic exposures they are all recommended for testing.

The major use for both EEQ and PEQ is in fabric softeners for industrial and consumer applications. Consumer

product formulations typically contain from 3.5 to 8 percent dispersions of the active ingredient. EEQ also is reported to be used as an anti-static agent, corrosion control agent, foam stabilizer and emulsifier (Ref. 5, Procter and Gamble 1984b). During and after use, these compounds will be released to the environment, mostly in wastewater from clothes-washing operations.

Analogs of PEQ, which also may be used as fabric softeners, and that are included in the recommended testing, are shown in the following Table 5:

TABLE 5—ADDITIONAL ETHOXYLATED QUATERNARY AMMONIUM COMPOUNDS RECOMMENDED FOR TESTING IF USED IN SUBSTANTIAL QUANTITIES IN FABRIC SOFTENING APPLICATIONS

CAS No.	Chemical name
68389-88-8	Poly(oxy-1,2-ethanediyl), α-[2-[bis(2-aminoethyl)methylammonio]ethyl]-ω-hydroxy-, N,N'-dicoco acyl derivs., Me sulfates (salts)
68389-89-9	Poly(oxy-1,2-ethanediyl), α-[2-[bis(2-aminoethyl)methylammonio]ethyl]-ω-hydroxy-, N,N'-bis(hydrogenated tallow acyl) derivs., Me sulfates (salts)
68413-04-7	Poly[oxy(methyl-1,2-ethanediyl)], α-[2-[bis(2-aminoethyl)methylammonio]methyl-ethyl-ω-hydroxy—, N,N'-ditallow acyl derivs.
68554-06-3	Poly(oxy-1,2-ethanediyl), α-[3-[bis(2-aminoethyl)methylammonio]-2-hydroxypropyl]-ω-hydroxy-, N-coco acyl derivs., Me sulfates (salts)
70914-09-9	Poly(oxy-1,2-ethanediyl), α-[2-[bis(2-aminoethyl)methylammonio]ethyl]-ω-hydroxy-, N,N'-di-C_{14-18} acyl derivs., Me sulfates (salts)

B. Evidence for Exposure

1. *Evidence for human exposure.* General population exposure to PEQ may be high given its use in fabric softeners. Ethoxylated quaternary ammonium fabric softeners are used in detergent formulations and in products designed for addition to washing machines prior to the last deep rinse of the wash cycle. The major route of exposure is skin contact with fabrics that have been treated with the fabric softener. Consumers who use these types of fabric softeners are likely to be exposed almost continuously through skin contact with clothing, towels and bed linens. Procter and Gamble (Ref. 5, 1984b) estimated daily consumer exposure to a "similar compound," from clothing to skin to be 0.07 mg active compound per kg per day for adults and 0.14 mg active compound per kg per day for children, assuming EEQ is deposited on fabrics at 0.17 mg/in^2. Sherex (Ref. 8, 1987) indicated that PEQ and EEQ are similar chemically and with respect to use. Therefore, the exposure estimates made by Procter and Gamble for EEQ appear to be applicable to PEQ.

An assessment by the Office of Toxic Substances (Ref. 1, Battin, 1988b) estimated annual consumer dermal exposure to this kind of compound, from exposure to softened clothing, linens, etc, at 1.08 to 2.69 g per year. Human exposure via drinking water is not expected to be significant. The ethoxylated quaternary ammonium compounds are expected to sorb strongly to sediments and other solids in surface waters and soils. Surface and ground waters used for drinking water will receive treatment (e.g., flocculation and sedimentation) that will further reduce the concentration of dissolved ethoxylated quaternary ammonium compounds. It has been estimated that surface waters used for drinking water supplies would contain no more than 0.35 μg/L of these compounds (Ref. 5, Procter and Gamble, 1984b).

2. *Evidence for environmental exposure.* No monitoring studies were found. An assessment by the Office of Toxic Substances (Ref. 1, Battin, 1988b) estimated receiving stream concentrations of 0.03 to 0.25 ug/L at manufacturing sites and 0.02 to 18.5 ug/L near use sites, depending upon location and stream flows. Procter and Gamble (Ref. 5, 1984b) estimated that consumer uses of EEQ would yield raw wastewater concentrations of about 280 ug/L. Most (95 percent or more) will be sorbed by sludge solids during wastewater treatment and the concentration of EEQ in treatment plant effluents was estimated at 35 ug/L.

II. Chemical Fate Information

A. *Transport*

The physical and chemical properties of the ethoxylated quaternary ammonium compounds indicate that they will partition strongly to sludge solids and organic sediments. The estimated low vapor pressure and moderate solubility in water rule out volatilization as an important factor. The cationic nature of these compounds will contribute to their sorption to sludge and sediment solids which generally are negatively charged.

B. *Persistence*

No published information was found on the persistence of the ethoxylated quaternary ammonium fabric softeners. A summary report of unpublished information (Ref. 5, Procter and Gamble, 1984b) showed 24 to 34 percent biodegradation after 138 days, using EEQ at 10 and 100 ug/L in river water and following carbon dioxide evolution. BOD studies using PEQ reported by Sherex (Ref. 7, 1984) showed 18 percent of theoretical oxygen uptake after 5 days and 31 percent after 30 days. While this indicates that EEQ and PEQ are biodegradable under aerobic conditions in river water, it also indicates that aerobic biodegradation will be relatively slow. The Procter and Gamble report (Ref. 5, 1984b) noted that the river water biodegradation studies were conducted with and without sediment but did not provide details. These quaternary ammonium compounds are expected to partition to sediments following release to the environment and their persistence in sediments, under both aerobic and anaerobic conditions, is unknown. Also unknown is the persistence of these compounds under conditions found in estuaries and the ocean. Persistence in saline water may be different than in fresh water. Nitrilotriacetic acid, for example, was found to be resistant to biodegradation in estuarine waters (Ref. 3, Bourquin and Przybyszewski, 1977) although it is readily biodegraded by acclimated microorganisms in fresh water.

C. *Rationale for Chemical Fate Recommendations*

EEQ, PEQ and PEQ analogs are likely to sorb strongly to waste treatment sludges and receiving stream organic sediments and may persist for relatively long time periods following sorption. Since they are being continuously released to both fresh water and estuarine receiving waters and may persist for relatively long periods of time there may be a tendency for these compounds to accumulate in estuarine, river and lake sediments near discharge points, with gradually increasing concentrations. There is a need to better define the persistence of these compounds, under both aerobic and anaerobic conditions, when sorbed to organic sediments typical of both freshwater and estuarine conditions. This information is needed in order to better assess the potential concentrations of these compounds in the sediments and the potential hazard to benthic organisms.

III. Biological Effects of Concern to Human Health

A. *Metabolism and Toxicokinetics*

No information was found.

B. *Acute and Subchronic (Short-term) Effects*

Summary reports on unpublished data from acute oral, percutaneous, ocular, skin irritation and subchronic toxicity

studies with EEQ were submitted by Procter and Gamble (Ref. 5, 1984b; Ref. 6, 1988). Data on acute oral, eye irritation, skin irritation and skin sensitization studies with PEQ were submitted by Sherex (Ref. 7, 1984). Data from acute oral, eye irritation and primary skin irritation studies with PEQ were provided by Capital City Products (Ref. 4, 1987).

The acute oral tests with EEQ and PEQ were all conducted using rats. Studies with EEQ yielded a minimum lethal dose greater than 15 g/kg. Studies with a 4 percent dispersion of PEQ showed an LD_{50} greater than 15.38 g/kg.

Minimal eye irritation was observed for EEQ instilled in the conjunctival sac of rabbit eyes unrinsed after treatment. PEQ was rated minimally irritating after instillation to unrinsed rabbit eyes.

Percutaneous studies with undiluted EEQ applied occluded to clipped intact and abraded backs of rabbits at dose levels of 2 g per kg for 24 hours yielded a minimum lethal does greater than 1.5 g per kg (the only dose tested) with a 14-day post-application period for mortality.

EEQ was applied occluded or on an open patch to clipped intact and abraded rabbit backs for 24 hours. Mild to moderate skin irritation was observed for up to 48 hours after patch removal. PEQ was applied to gauze patches and exposed to clipped intact and abraded rabbit backs for 24 hours. The substance was rated mildly to severely irritating following observations at 24 and 72 hours.

A skin sensitization study reported by Procter and Gamble (Ref. 5, 1984b) employed 25 percent (w/v) EEQ in 80:20 ethanol: Water solution applied in occluded patches to the clipped backs of guinea pigs for six hours, once a week, during a three-week induction period. The EEQ treated animals were challenged with 20 percent (w/v) EEQ in acetone for a single 6-hour occluded exposure approximately two weeks after completion of induction. Five out of 20 induced guinea pigs showed signs of delayed contact hypersensitivity. These studies led to the conclusion with EEQ is a mild skin sensitizer in guinea pigs. Similar studies reported by Sherex (Ref. 7, 1984) concluded that PEQ is not a skin sensitizer.

In a subchronic toxicity study (Ref. 5, Procter and Gamble, 1984b) rabbits were treated topically with 2 mL per kg per day of EEQ at a dose level of 300 mg of active compound per kg per day, five days per week for 4 weeks. Each group contained five males and five females. There were no treatment-related changes in body weights, body weight gain, organ weights or organ to body weight ratios. It was also reported that there were no treatment-related clinical changes. However, animals receiving EEQ had significantly greater mean corpuscular volumes in week 4 than the controls and there was an increased incidence of dermal inflammation, of diffuse distribution and associated with acanthosis, that was considered treatment-related. An increased incidence of dermatitis was attributed to "random variation."

C. Genotoxicity

In summary reports it was stated that EEQ was tested for mutagenicity in the *Salmonella* assay, with and without metabolic activation, and the mouse lymphoma assay (Ref. 5, Procter and Gamble 1984b) and that those tests produced negative results. No information was found for PEQ or the other ethoxylated quaternary ammonium compounds recommended in this Report.

D. Oncogenicity

No information was found.

E. Reproductive and Developmental Effects

No information was found.

F. Chronic (Long-term) Effects

No information was found.

G. Observations in Humans

Little or no irritation was observed with human volunteers in a skin irritation test with aqueous dispersions of EEQ using 0.3 mL of EEQ per occluded patch (Ref. 5, Procter and Gamble, 1984b). EEQ was tested in a single 24-hour and three 24-hour exposures over a 6-day period at concentrations up to 20 percent (w/v). In another Procter and Gamble study (Ref. 5, 1984b), 87 volunteers received 9 exposures to 10 percent (w/v) aqueous EEQ and 205 volunteers received 9 exposures to 25 percent (w/v) aqueous EEQ (0.3 mL per occluded patch) applied for a 24-hour period, 3 times a week during a 3-week induction period. No skin sensitization was observed when subjects were challenged two weeks later with a single 24-hour occluded patch with the same concentration used during induction.

H. Rationale for Health Effects Recommendations

It has been estimated that fabric softeners that are applied to fabrics during the washing process are widely used in the U.S. Annual U.S. consumption of the ethoxylated quaternary ammonium type fabric softeners has been estimated at about 25 million pounds. It is quite apparent that a significant portion of the population is exposed, on a nearly continuous basis, to these chemicals in clothing, toweling and bed linens. Exposure will be primarily dermal although there may be very low concentrations in some drinking water supplies. Dermal exposure tests reported to date have involved only acute or short-term exposures. EEQ was described as a mild to severe irritant and PEQ was mildly irritating when applied to rabbit skin. EEQ was a mild skin sensitizer in some guinea pig studies.

Although exposure concentrations used in short-term studies were reported to be several-fold higher than estimated human exposures from softened fabrics, information from these short-term, intermittent-exposure tests is not useful in predicting what effects might occur with long-term (years) continuous exposure. It is therefore recommended that EEQ, PEQ and commercially important analogs of PEQ be tested for chronic toxicity to evaluate potential effects resulting from long-term dermal exposure.

IV. Ecological Effects of Concern

A. Acute and Subchronic (Short-term) Effects

Summary data submitted by Procter and Gamble (Ref. 5, 1984b) show EEQ toxicity to bluegills, sheepshead minnows, mysid shrimp and *Daphnia magna* water fleas, with LC_{50} values ranging from 0.3 to 45 mg/L. The presence of an anionic surfactant or the use of natural surface waters with sediments mitigated the effects on bluegills and daphnia. No data were found for benthic organisms and this is a data gap of concern since these compounds are likely to partition to sediments following release to the environment. No data were found for PEQ or its analogs.

B. Chronic (Long-term) Effects

No information was found.

C. Other Ecological Effects (Biological, Behavioral or Ecosystem Processes)

EEQ was reported to inhibit algal growth at moderately low concentrations (Ref. 5, Procter and Gamble, 1984b). The algistatic concentrations were 1.33 mg/L for a *Selenastrum* sp., 0.52 mg/L for a *Mycrocystis* sp., and 9.4 mg/L for a *Dunaliella* sp. No data were found for PEQ or its analogs.

D. Bioconcentration and Food-chain Transport

The measured log P of 2.48 for EEQ indicates a potential for some bioconcentration. Procter and Gamble (Ref. 5, 1984b) reported an estimated bioconcentration factor (BCF) of 45 for EEQ, based on the log P. No information was found for PEQ or its analogs.

E. Rationale for Ecological Effects Recommendations

Environmental fate considerations indicate that the ethoxylated quaternary ammonium compounds will sorb strongly to sludge solids and sediments. They may persist for relatively long periods of time under those conditions and accumulate in sediments in the vicinity of wastewater discharges. This information plus the demonstrated toxicity of EEQ to fish, aquatic invertebrates and algae, raise concerns for benthic organisms. Acute toxicity should be determined for representative freshwater and estuarine benthic organisms and, if the ethoxylated quaternary ammonium compounds are found to be relatively persistent in the environment, chronic studies on the same organisms may be warranted.

References

(1) Battin, A. Memorandum on exposure and release of ethoxylated quaternary ammonium compounds in liquid fabric softeners from Andrew Battin, Exposure Assessment Branch, Office of Toxic Substances, U.S. Environmental Protection Agency, to John D. Walker, Test Rules Development Branch. (February 2, 1988b).

(2) Battin, A. Memorandum on physical/chemical property estimations from Andrew Battin, Exposure Assessment Branch, Office of Toxic Substances, U.S. Environmental Protection Agency, to Robert Brink, TSCA Interagency Testing Committee (April 8, 1988c).

(3) Bourquin, A.W. and Przybyszewski, V.A. "Distribution of bacteria and nitrilotriacetate-degrading potential in an estuarine environment," *Applied and Environmental Microbiology*. 34:411–418 (1977).

(4) Capital City Products. Letter and unpublished information from John B. Braunwarth, Operations Manager, Capital City Products Co. Janesville, WI, to Robert Brink, TSCA Interagency Testing Committee (February 18, 1987).

(5) Procter and Gamble. Letter and unpublished information from T.W. Mooney, Manager, Technical Government Relations, The Procter and Gamble Co., Cincinnati, OH, to Arthur Stern, TSCA Interagency Testing Committee (September 12, 1984b).

(6) Procter and Gamble. Letter from R.N. Sturm, Associate Director, Bar Soap and Household Cleaning Product Development, Procter and Gamble Co., Cincinnati, OH, to Robert Brink, TSCA Interagency Testing Committee (April 19, 1988).

(7) Sherex. Unpublished information submitted from Howard M. Hickman, Sherex Chemical Co., Inc., Dublin, OH, to Martin Greif, TSCA Interagency Testing Committee (January 17, 1984).

(8) Sherex. Personal communication from Howard Hickman of Sherex Chemical Co., Inc. Dublin, OH, to L. Borghi, Dynamac Corporation (January 13, 1987).

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